Pacific Biomarkers
The Value of Expertise

Bile Acids, Total

Analyte: Total Bile Acids
Specimen Type: EDTA Plasma
Optimum Volume: 0.25 mL
Stability:

2-8 Degrees C	-20 Degrees C	-70 Degrees C
1 day	3 months	3 months

Reporting Units: umol/L
Method: Enzymic

Biological or Clinical Significance:
Bile acids are 24-carbon steroids formed from cholesterol in the liver. Five major bile acid forms compose over 99% of the bile acid pool formed in body fluids.

The liver synthesizes two primary bile acids, cholic acid and chenodeoxycholic acid from cholesterol. The primary bile acids are converted to the secondary bile acids, deoxycholic acid and lithocholic acid, by intestinal bacteria. A fraction of chenodeoxycholic acid is also transformed into tertiary bile acid, ursodeoxycholic acid, in the liver. All bile acids secreted by the liver are conjugated with an amino acid, either with glycine or with taurine. The conjugated bile acids form further complexes with sodium to become bile salts.

In clinical diagnosis, TBA (total bile acid) testing refers to the testing of the sum of all these forms of bile acid conjugates (primary, secondary and tertiary bile acids and their conjugates).

The average bile acid composition of healthy human adult bile is 38% cholate conjugates, 34% chenodeoxycholate conjugates, 28% deoxycholate conjugates, and 1-2% lithocholate conjugates.

Bile acids are the major constituent of bile, and in mammals, compose approximately 67% of bile secretion. Bile acids are released from the liver as conjugated salts into the small intestine via the bile duct during intestinal contraction. Bile acids are lipid-carriers and are able to solubilize many lipids by forming mixed micells with fatty acids, cholesterol for the solubilzation and absorption of fat-soluble vitamins such as vitamin E. The ability of bile acids to solubilize cholesterol in bile is the major mechanism of cholesterol elimination from the body to prevent cholesterol elimination from the body to prevent cholesterol accumulation with the attendant risk of artherosclerosis.

More than 90% of the bile acids are actively reabsorbed (by a sodium dependent co-transport process) from the ileum into the hepatic portal circulation from where they are cleared and re-secreted by the liver to be stored in the gallbladder. The bile acids pool cycles 5 – 10 times daily through the enterohepatic circulation. The liver normally clears 20 g of bile salt from the blood each day.

Normally, the liver is very efficient at capturing and removing bile acids from the hepatic-portal circulation. This is why the peripheral blood levels of total bile acids are quite low in healthy subjects.

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However, when the enterohepatic circulation system is impaired, bile acid levels in the blood are increased as a result of diminished hepatic elimination of bile acids from the portal blood, which results from diminished hepatic clearance and from portosystemic shunting.

Serum or plasma TBA levels are sensitive indicators of liver function in all species, reflecting both hepatic synthesis, secretion, and re-absorptive functions. Therefore, testing for TBA will help to detect liver functional changes before the formation of more advanced clinical signs of illness such as icterus. This early sensitivity is very important in clinical diagnosis because it allows for the possibility of treatment before extensive and irreversible damage is done. Studies in humans with various liver diseases show that TBA can be used to assess hepatic dysfunction with valuable information that is not provided by conventional tests on serum levels of liver enzymes such as ALT and AST. However, the test will not provide a definitive diagnostics of the primary problem, merely an early confirmation that there is hepatobilliary deficiency.

Principle of Test Method:

The cycling assay is a method that allows for signal amplification through cycled regeneration reactions. In the enzyme cycling based TBA assay, serum bile acids molecules are repeatedly oxidized and reduced by the enzyme 3-α-hydoxysteroid dehydrogenase (3-α-HSD) with a concomitant accumulation of reduced co-enzyme thio-NADH that is detected at a specific wavelength (405 nm).

In the forward reaction, the enzyme catalyzes the oxidation reaction in the presence of the co-enzyme thio-NAD+ to form oxidized bile acids and reduced co-enzyme thio-NADH. On the other hand, in the reverse reaction, the enzyme catalyzes the reduction reaction in the presence of excess co-enzyme NADH to convert oxidized bile acids back to bile acids, which are then ready for the next round of forward oxidation reaction.